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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/638,647	08/14/2000	David M. Stern	0575/62176/JPW/JML	9844

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John P White
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER
CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n N .	Applicant(s)	
	09/638,647	STERN ET AL.	
	Examin r	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *August 14, 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's arguments filed March 31, 2003 in paper no. 8 have been fully considered but they are not persuasive. The amendments have been entered. Claims 1-8 are pending.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose genome comprises a DNA sequence comprising a nerve tissue specific promoter operatively linked to a DNA sequence encoding ABAD and a nerve tissue specific promoter operably linked to an alternatively spliced hAPP mini-gene that encodes hAPP695, hAPP751 and hAPP770 comprising one or more familial Alzheimer's disease mutants and methods of using the mice to evaluate therapeutic treatments, does not reasonably provide enablement for a transgenic nonhuman animal comprising separate DNA sequences encoding hAPP695, hAPP751 and hAPP770 and methods of evaluating using the transgenic nonhuman animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues that the examiner has not made the improper incorporation rejection, with regard to Hsia (formerly Mucke), in connection with a specific claim, and thus they are not properly able to address the assertion that the mice of Hsia are critical to the invention. This argument is not persuasive.

The improper incorporation by reference rejection was made under the enablement portion of 35 U.S.C., and claims 1-8 were included in the rejection. Applicant was clearly told which claims were so rejected.

Applicant argues that the examiner asserts that the production of ABAD/hAPP transgenic mice with the claimed phenotype would be unpredictable. Applicant argues that the art, as evidenced by Moechars, teaches that the behavioral and cognitive defects that have been observed and documented are shared in all APP transgenic mouse lines, that there are common and consistent early defects in all APP transgenic mouse lines presented by them and reported by others, and 3) their study demonstrates that with the exception of amyloid plaques, the qualitative differences between transgenic mouse lines. This argument is not persuasive.

The rejection is directed to the breath of the claims to "transgenic animals" and transgenic rat, sheep, dog, primate or reptile. The examiner would agree that transgenic ABAD/hAPP mice, if the starting transgenic mice were readily available, would exhibit the phenotypes claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons set forth in the office action mailed September 24, 2002.

Claims 1 and 5 state in part (b) that the mouse contains "... a DNA sequence encoding a mutant human amyloid precursor protein HAPP695, hAPP751 and hAPP770 ..." This phrase is confusing as each APP listed is a splice variant of APP. It is not clear if applicant means the DNA sequence gives rise to all three splice variants in the doubly transgenic mice.

Applicant argues that at page 32, lines 30 and 31 of the specification discloses that the hAPP transgenic mice overexpresses an alternatively spliced hAPP minigene that encodes hAPP695, hAPP751 and hAPP770 bearing familial AD mutations. Applicant contends that this makes it clear that the mouse expresses all three splice variants. These arguments are not persuasive.

At the citation, the specification states, " the Tg mice overexpress an alternatively spliced hAPP mini-gene that encodes hAPP695, hAPP751 and hAPP770 bearing mutations ...". However, the language of claims 1 and 5 do not reflect the alternative splicing.

Claims 1 and 5 state ABAD is amyloid-beta peptide alcohol dehydrogenase. The art defines an ABAD as amyloid-beta peptide binding alcohol dehydrogenase and as amyloid beta binding alcohol dehydrogenase. Are these the same dehydrogenases. Because the names and function appear to be similar, it is confusing as to the relation of the enzymes.

Applicant argues that they are not aware that a term set forth in a claim must be identical to all others in the art used to describe the same entity, as long as the claims set for the metes and bounds of the invention. Applicant argues that one of skill in the art would know the metes and bounds of the claims. This argument is not persuasive.

In this particular instance, there is confusion as to the definition of ABAD. The only reference to DNA sequences or amino acid sequences encoding amyloid beta peptide binding alcohol dehydrogenase is at pages 9, line 17 to page 12, line 7. Applicant has not explained how the skilled artisan would know the metes and bounds of the claims with regard to ABAD.

The claims are free of the prior art. The prior art did not teach or suggest transgenic nonhuman animals whose cells contain a DNA sequence comprising a nerve tissue specific promoter operatively linked to a DNA sequence which encodes amyloid-beta peptide alcohol dehydrogenate and a DNA sequence comprising a nerve tissue specific promoter operatively linked to a DNA sequence encoding a mutant human amyloid precursor protein hAPP695, hAPP751 and hAPP770 bearing mutations linked to familial Alzheimer's Disease in human, wherein said nonhuman animal exhibits at least one phenotype from the group consisting of: reduced basal synaptic transmission, inhibited synaptic plasticity, increased neuronal stress, elevated 4-hydroxynoneal in cerebral cortex, increased heme oxygenase type I in cerebral cortex, decreased synaptophysin in cerebral cortex, decreased microtubule-associated protein-2 in cerebral cortex, and increased levels of activated caspase 3 antigen in cortical neurons, or methods of using these mice in methods for evaluating the potential therapeutic effect of an agent for treating Alzheimer's Disease.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on Mon.-Thur., 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
May 22, 2003